Full Text

Journal of the American Veterinary Medical Association
May 15, 2017, Vol. 250, No. 10, Pages 1155-1166
https://doi.org/10.2460/javma.250.10.1155

A literature review on the welfare implications of gonadectomy of dogs

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ABSTRACT

In the United States, dogs not intended for breeding are routinely neutered via elective gonadectomy (OHE or castration), resulting in 86% of owned dogs being spayed or neutered.[1] In addition to the fact that gonadectomy renders dogs infertile, removal of sex hormones produced by the gonads may influence the incidence of a variety of disease processes. The risks and benefits of gonadectomy are constantly being examined, which has resulted in renewed conversations about if and when to neuter animals. This has created a challenging environment for companion animal practitioners striving to make the best decisions for their patients.

In a joint position statement,[2] the American College of Theriogenologists and Society for Theriogenology assert that companion animals not intended for breeding should be spayed or neutered, although the decision must be made on a case-by-case basis and take into consideration the pet's age, breed, sex, intended use, household environment, and temperament. Developing recommendations for an informed case-by-case assessment requires an evaluation of the risks and benefits of gonadectomy, including potential effects on neoplasia, orthopedic disease, reproductive disease, behavior, longevity, and population management as well as the risks of anesthetic and surgical complications. However, many factors other than neuter status play an important role in these outcomes, including breed, sex, genetics, lifestyle, and body condition. Potential consequences for an individual animal must also be weighed with the necessity of managing unwanted pet populations. Because of the aforementioned variables, there currently is no single recommendation regarding gonadectomy that would be appropriate for all dogs. The information reported here summarizes the currently available literature involving risks and benefits that might be considered when making a recommendation about gonadectomy of dogs and the optimal age for performing the procedure.

ABBREVIATIONS

BPH Benign prostatic hyperplasia

CCL Cranial cruciate ligament

OHE Ovariohysterectomy

VMDB Veterinary Medical Databases

Considerations During Evaluation of the Available Literature

Inconsistencies in patient categorization of various studies make it difficult to synthesize the overall data set. Depending on the study, early gonadectomy can be defined in a variety of ways, including surgery prior to 5.5 months of age[3,4] or before 1 year of age.[5–7] Age at gonadectomy was unavailable for other studies[8–10] that differentiated only between sexually intact and neutered dogs.

Many of the existing reports are retrospective studies. Although the number of available cases is often quite high, the source for the cases in a study can result in an inherent selection bias. The VMDB selects for patients cared for at referral hospitals, and members of breed clubs may represent an extremely different population than the animal population for typical pet owners.[11] Owners must elect to participate in surveys and also may have recall bias.[12]

Determining the incidence of diseases also poses a major challenge. Veterinary medicine lacks the population surveys used in human medicine to obtain a baseline incidence within the general population. Other than the VMDB, which contains cases limited to some veterinary teaching hospitals, most private, corporate, and specialty-referral practices manage their records independently. Owner preference or veterinarian recommendation may result in patients being treated for a disease or being euthanized without a definitive diagnosis. Additionally, the information on incidence in pathology studies may differ because some diseases may represent incidental findings and specimens are limited to owners who elect for biopsy or necropsy.

The multifactorial nature of many diseases interferes with determining the underlying reason why there may be a link to neuter status or timing of gonadectomy.[11] The etiology of many diseases is not definitively known, which makes it difficult to evaluate the potential effects of sex hormones. Furthermore, detecting an association does not indicate causation. A deeper understanding of how the presence or absence of sex hormones affects each disease process is needed before more concrete conclusions can be made about the influence of gonadectomy on overall health.

Relative risk and OR serve as a measure of the strength of the association between a disease and exposure to a factor (in this case, gonadectomy).[12] Relative risk is the ratio of 2 risks (usually the ratio of the risk of disease in an exposed group to the risk of disease in an unexposed group). It provides a measure of the strength of the association between the disease and exposure to the factor. If the relative risk is 1.0, then exposure to the factor does not affect an animal's chance of developing the disease; a relative risk > 1.0 indicates an increased risk for developing the disease associated with exposure to the factor. In contrast, the OR is the ratio of 2 odds (usually the odds of disease in a group exposed to a factor divided by the odds of disease in an unexposed group). It represents an estimate of the relative risk when the disease is rare.

The importance of an increased relative risk must be considered along with the overall prevalence of the condition within the population.[11] An increased relative risk for a more common neoplasia such as lymphoma has the potential for greater consequences than does an increased relative risk for a rare disease such as uterine neoplasia. Another example is the rarity of prostate neoplasia in male companion animal dogs, which effectively negates concerns a veterinarian might have that neutering of male dogs will cause prostate neoplasia.[13]

In addition to the frequency of disease, severity of the disease and availability of effective treatments are also considerations when weighing the risks and benefits of gonadectomy for an individual animal. Potentially increasing the likelihood of an easily managed disease process such as urinary incontinence is outweighed by the desire to minimize risk for the development of mammary gland neoplasia. Practitioners also must consider potential effects on overall quality of life as well as morbidity and mortality rates.

Breed-specific studies are valuable to veterinarians who work with those breeds, but the information cannot be extrapolated and applied to all dogs.[11] Contrary to the association between neoplasia and gonadectomy in Golden Retrievers, there is not a significant correlation between neutering male or female Labrador Retrievers or German Shepherd Dogs at any age and the development of several neoplasms (lymphosarcoma, hemangiosarcoma, or mast cell tumor).[5,6,14] Further research focusing on specific breeds and also on broader groups of dogs will be important for making recommendations about individual patients. Currently, it is important to acknowledge the large role that genetics and breed play in disease processes when developing recommendations.[15,16]

Breeding practices may also impact the data. Animals with an increased incidence of neoplasia, orthopedic disease, or undesirable behaviors may be less likely to be chosen as stud dogs. As a result, those dogs and their offspring that are at higher risk genetically may be neutered to prevent passage of the disease risk to progeny.

Neoplasia

Neoplasia represents a major cause of morbidity and fatalities for companion animals and is a leading cause for concern among dog owners.[16,18] Factors contributing to the development of neoplasia may include, but are not limited to, genetic predisposition, breed, age, viral infection, environment, chronic inflammation, and neuter status. Gonadectomy has the potential to decrease the incidence of certain types of neoplasia and increase the incidence of others. When the risks and benefits of gonadectomy related to neoplasia are evaluated, consideration must be given to the morbidity and mortality rate for each neoplastic disease as well as its prevalence within the general canine population or a specific breed.

Mammary gland tumors are the most common neoplasia in female dogs.[16,19–23] The incidence of mammary gland neoplasia in dogs in the United States (3.4%) is significantly lower than that in other countries in which OHE is typically used only as a treatment of uterine diseases in older dogs.[19,21,23–28] For instance, mammary gland neoplasia accounted for 70% of all cases of neoplasia evaluated in the municipality of Genoa, Italy, between 1985 and 2002, and the incidence of malignant mammary gland tumors in Norway was 53.3%.[21,23]

Because 35% to 51% of mammary gland tumors of dogs are malignant, they represent the most common malignant tumors in dogs.[20,28–31] In addition to local invasion and ulceration of primary tumors, malignant tumors have the potential to metastasize, most commonly to the regional lymph nodes and lungs.[19,28,29,31,32] This combination of a high incidence and malignancy represents a substantial risk to the female canine population. Age, hormonal exposure, and breed are the 3 main factors that contribute to the risk of developing mammary gland tumors, whereas diet, body weight, and obesity may play smaller roles.[19,24,30,33]

Breed influences the incidence of mammary gland neoplasia.[16,21,25,29,30,34,35] These reports are supported by more recent breed-specific literature. In a retrospective study[5] conducted to evaluate Golden Retrievers and the follow-up study[6] conducted to compare results for Golden Retrievers and Labrador Retrievers, extremely few dogs had mammary gland neoplasia regardless of neuter status. This could have been affected by the age of patients included in the studies because the mean age for development of malignant mammary gland tumors is approximately 9 to 11 years,[11,24,28,35] and the 2 aforementioned studies[5,6] only included patients up to 8 years of age. However in retrospective studies focusing on Vizslas[36] and German Shepherd Dogs[14] through at least 11 years of age, mammary gland neoplasia remained much less common than the other neoplasias.

Compared with spayed bitches, sexually intact females have a higher incidence (3 to 7 times as high) of mammary gland tumors.[33,35] Historically, there has been general agreement that spaying has the greatest benefit for prevention of mammary gland tumors if performed prior to the first estrus. A protective effect of OHE is indicated by the fact that the relative risk of mammary gland tumors for bitches spayed before their first estrus is 0.05%, compared with that for sexually intact bitches, which then increases to 8% when spayed after the first estrus and 26% when spayed after the second estrus.[37] Subsequent studies[20,30,38,39] have continued to support the protective effect of early spaying. The connection between exposure to exogenous progesterone and an increased risk of developing malignant mammary gland tumors further supports the association.[11,40] Hormonal influences from pregnancy or estrus beyond the initial 2 estrous cycles have not been found to significantly contribute to an increased risk of malignant mammary gland tumors.[19,34,37] Recently, the protective benefit of spaying was challenged when a systematic review of the related literature was unable to identify a strong association between spaying and development of mammary gland tumors.[41] However, that review was based on meta-analyses in human medicine, which required a massive body of literature that currently does not exist in veterinary medicine[11,42]; thus, the review[41] of spaying and development of mammary gland tumors may have reflected a lack of statistical power in the analysis.

Ovarian tumors of the bitch are uncommon, although it has been difficult to determine the incidence in part because of the routine practice of OHE in the United States.[1,43–47] The overall prevalence of ovarian tumors reported is 0.5% to 1.4%[44–47] but is potentially as high as 6.25% when including histologic evaluation.[46,48] Age of occurrence, rate of metastasis, and frequency of concurrent uterine malignancy or endocrine disease are dependent on the type of neoplasia.[44–47,49] Ovariectomy or OHE would be preventive and is the mainstay of treatment, but gonadectomy would only be helpful for benign or localized ovarian tumors.[11,43] The prognosis is poor for patients with malignant neoplasia with evidence of metastatic disease, which can occur in up to 50% of cases.[44,49]

Uterine neoplasms are rare, accounting for 0.3% to 0.4% of all neoplastic conditions in dogs; benign mesenchymal tumors and leiomyomas are the most common types of uterine neoplasms.[29,43,50,51] Leiomyomas are generally slow growing, noninvasive, and nonmetastatic.[43,50] Because most uterine neoplasms in dogs are benign, OHE is the treatment of choice and often is curative.[29,44]

Vaginal and vulvar tumors account for 2.4% to 3% of all tumors of dogs.[44,51,52] Leiomyomas are the most common vaginal tumors of dogs.[34,44,50] Because they most commonly develop in sexually intact bitches, it is suggested that vaginal leiomyomas may be hormone dependent.[44,50] Although this association has not been proven, OHE may have a substantial sparing effect. For benign tumors, OHE used as an adjunct treatment to surgical excision of the primary vaginal or vulvar tumor is almost always curative.[34,43,44,50,51]

Transmissible venereal tumors of dogs are transmitted primarily by coitus.[53–55] Consequently, free-roaming sexually intact dogs are at greatest risk.[54,55] In enzootic areas where breeding is poorly controlled and there are high numbers of free-roaming sexually active dogs, transmissible venereal tumor is the most common tumor of dogs.[53–55] Transmissible venereal tumors generally remain localized to the external genitalia.[53–55] Tumors can become locally invasive, and metastasis occurs in up to 5% to 17% of affected dogs.[54,55] A decrease in mating behavior within a population as a result of gonadectomies would greatly reduce the occurrence of transmissible venereal tumors.

Testicular tumors are a common neoplasia, accounting for up to 16% to 27% of tumors of sexually intact male dogs and approximately 90% of all tumors in the male reproductive tract.[56–60] Unilateral testicular enlargement with atrophy of the contralateral testis is often evident, but metastasis is rare.[28,56,61] Bilateral castration serves as both a preventive measure and the treatment of choice for most testicular tumors and is typically curative.[11,43,50,57,61] Because cryptorchidism is hereditary and intra-abdominal cryptorchid testes are strongly associated with testicular neoplasia, cryptorchid dogs should be castrated.[43,57,58,60,61]

Prostatic carcinoma of dogs is aggressive and characterized as locally invasive with high metastatic potential.[43,50,62] Although prostate neoplasia is seen more often in dogs than in other domestic species, prostate neoplasia is considered rare in dogs, with an estimated prevalence of 0.29% to 0.6%.[11,13,16,43,63–66] In the past, castration was recommended as part of treatment and viewed to have the potential to decrease the risk of prostatic carcinoma.[34,50,63] More recent studies[13,67,68] have shown castration to be a risk factor for development of prostate neoplasia in male dogs, with the OR ranging between 3.6 and 4.34 for prostatic carcinoma. The age at castration may not have an effect on when prostatic carcinoma develops because the interval between castration and onset of prostatic problems is highly variable.[67] Also, the age at which prostate neoplasia was diagnosed was older for neutered dogs or did not differ significantly between sexually intact and neutered dogs.[13,67] Risk of developing prostate neoplasia also differs among breeds.[13,34,67]

Although tumors of the bladder and urethra are rare in dogs, accounting for approximately 2% of neoplasms in dogs, invasive transitional cell carcinoma is the most common type.[43,69–73] Transitional cell carcinomas in dogs are highly malignant, and local metastasis is common.[43,69] Associations have been made between these tumors and breed, female sex, obesity, environmental factors, and possibly cyclophosphamide.[16,43,69,70,72–75] Gonadectomy also appears to increase the risk for developing transitional cell carcinomas, although the reason for this increase has not been determined.[13,69,71,72] For neutered male dogs, the relative risk for the development of transitional cell carcinomas of the urinary bladder and prostate was found to be 3.56 and 8.00, respectively, compared with the relative risks for sexually intact male dogs.[13] Investigators of a retrospective study[71] of 155 dogs reported that gonadectomized dogs were at an increased risk (OR, 2.03) of developing tumors of the lower urinary tract. The prognosis for the patients evaluated in that study was poor, with only 16% surviving ≥ 1 year. Most dogs were untreated and euthanized at the time of neoplasia diagnosis or subsequently died of the disease.[71]

Lymphoma is one of the most commonly diagnosed neoplasias of dogs.[16,23,76–79] The prognosis for individual dogs differs widely. Although rarely curable (< 10% of cases), complete remission can be achieved with conventional chemotherapy in 60% to 90% of affected dogs.[76,77,79,80] Good quality of life is typically maintained during extended remissions of 6 to 13 months.[76,77,80] Associations have been made between the development of lymphoma and breed as well as environmental, immunologic, and hormonal factors; however, the etiology is likely multifactorial and largely unknown.[16,76,77,79,81,82] With regard to gonadectomy as a risk factor for lymphoma, a comparative medicine study[82] that involved use of data in the VMDB revealed that sexually intact male dogs and neutered male and female dogs were twice as likely as sexually intact female dogs to develop lymphoma. Similar results have been reported in human medicine, with men developing non-Hodgkin's lymphoma approximately 50% more often than women.[11,82] However, this association was not evident for the evaluation of the Animal Tumor Registry of Genoa, Italy, which revealed similar incidence rates of non-Hodgkin's lymphoma in male and female dogs.[23] Multiple breed-specific studies have related but inconsistent findings. For Vizslas, analysis suggested that both neutered males and females were 4.3 times as likely as their sexually intact counterparts to have lymphoma.[36] Sex was not found to be a risk factor for Vizslas irrespective of neuter status.[36] Gonadectomy of either sex did not affect the risk of lymphoma in Labrador Retrievers or German Shepherd Dogs.[6,14] In Golden Retrievers, there was not a significant risk of developing lymphoma associated with spaying females at any age.[5] Male Golden Retrievers neutered before 1 year of age were 3 times as likely as sexually intact males to develop lymphoma, but there were no cases of lymphoma in the group of male dogs neutered at > 1 year of age.[5]

Mast cell tumors comprise 16% to 21% of all cutaneous tumors of dogs.[8,27,78,83,84] Patient prognosis differs and is dependent on multiple factors, including histologic grade, tumor location, breed, and clinical stage of the disease at the time of diagnosis.[16,84–88] Although there is no apparent sex predilection, there is evidence that spayed females may have a higher relative risk of developing a mast cell tumor, compared with the likelihood for their sexually intact counterparts.[8,11,83,87] Investigators of a study[8] of dogs examined at the Animal Medical Center in New York reported an OR of 4.11 for spayed females to develop mast cell tumors, compared with the likelihood for sexually intact bitches, although the age at gonadectomy was unknown for that study. The odds of gonadectomized Vizslas of either sex developing mast cell tumors were 3.5 times the odds of sexually intact Vizslas developing mast cell tumors.[36] For Golden Retrievers,[5] Labrador Retrievers,[6] and German Shepherd Dogs,[14] there was not a significant difference between the incidence of mast cell tumors in males and females regardless of neuter status or time of gonadectomy. There are several breeds at an increased risk for developing mast cell tumors regardless of neuter status.[16,83,84]

Hemangiosarcoma represents approximately 5% to 7% of all noncutaneous primary malignant neoplasms of dogs.[16,30,78,89] The overall prognosis for dogs with hemangiosarcoma is extremely poor, with ≤ 10% surviving for 12 months, even when receiving adjunctive chemotherapy after surgery.[89–92] Although age at gonadectomy was unknown, a retrospective study[9] of splenic hemangiosarcoma and hematoma in various breeds revealed that spayed females have a significantly increased likelihood of developing hemangiosarcoma (OR, 2.2) when compared with the likelihood for sexually intact female dogs.

Hemangiosarcoma has also been evaluated in multiple breed-specific retrospective studies. Neuter status of male Golden Retrievers[5] and Vizslas[36] did not affect the overall likelihood of developing hemangiosarcoma. However, when only male Vizslas neutered at > 12 months of age were considered, they were 5.3 times as likely to develop hemangiosarcoma.[36] This increased risk in only late-gonadectomy dogs was mirrored in female Golden Retrievers spayed at > 1 year of age.[5] Those late-spayed females had hemangiosarcoma > 4 times as frequently as did sexually intact females and females spayed before 6 months of age.[5] Reasons that dogs neutered before 1 year old and sexually intact dogs have a similarly reduced risk for hemangiosarcoma, compared with the risk for female dogs neutered at > 12 months of age, are still being debated. Female Vizslas spayed at > 12 months of age had a higher risk (OR, 11.5) of developing hemangiosarcoma, compared with the risk (OR, 6.0) for those spayed before 12 months of age.[36] This was a significant increased risk for both groups of spayed Vizslas, compared with the risk for sexually intact females, which is in contrast to the results for Golden Retrievers.[5] It is important to mention that neuter status for Golden Retrievers and Labrador Retrievers of both sexes was not associated with a significant increased risk of developing hemangiosarcoma in a follow-up comparative study.[6] Gonadectomy also is not a risk for the development of hemangiosarcoma in German Shepherd Dogs.[14] Cardiac hemangiosarcoma was specifically evaluated in a retrospective study[93] that included data from the VMDB. In that study,[93] gonadectomized males and females of various breeds had overall relative risks of 1.6 and 4.38, respectively, compared with that of their sexually intact counterparts. The incidence of cardiac tumors in the total population was 0.19%.[93]

Osteosarcoma is the most common primary malignant bone tumor of dogs.[16,94–99] Osteosarcoma is locally aggressive and frequently has early metastasis, most often to pulmonary structures.[94,95,98–100] Metastatic disease is often subclinical and only apparent radiographically in < 15% of patients at initial examination.[94,95,98–100] Treatment can be intensive and often includes adjunctive therapy because approximately 90% of patients die of metastatic disease within 1 year when amputation is the only treatment.[94,95,98–100] Large- and giant-breed dogs are at greater risk of developing osteosarcoma.[10,16,94,98,99] Gonadectomy may also contribute to a higher risk of developing osteosarcoma.[7,10] A retrospective study[10] conducted with data from the VMDB confirmed that increasing breed size is a significant risk factor for osteosarcoma. Although age at gonadectomy was not available, gonadectomized dogs were twice as likely as sexually intact dogs to develop osteosarcoma.[10] A historical cohort study[7] for which investigators specifically evaluated Rottweilers revealed that risk for osteosarcoma was significantly influenced by both neuter status and age at gonadectomy. Male and female dogs that were neutered before 1 year of age had a risk that approximately 1 in 4 would develop osteosarcoma during their lifetime.[7] Furthermore, there is potentially an inverse association between lifetime exposure to gonadal hormones and risk of spontaneously developing osteosarcoma because dogs that developed osteosarcoma in that study[7] were sexually intact for significantly fewer months than were dogs that did not develop osteosarcoma. Neuter status or age at gonadectomy does not affect development of osteosarcoma in German Shepherd Dogs.[14]

Orthopedic Diseases

Musculoskeletal diseases such as CCL disease and hip dysplasia are not inherently life-threatening conditions, but they do affect physical performance and quality of life of patients. Surgical correction of CCL disease and hip dysplasia can also be cost prohibitive for owners. In situations whereby chronic orthopedic pain of animals cannot be adequately managed, especially in large-breed dogs, euthanasia may be considered. The incidence of CCL disease and hip dysplasia is 1.7% and 1.8%, respectively.[28] The true disease prevalence of hip dysplasia is difficult to determine because of selection bias for those dogs provided for evaluation or that are typically screened, membership bias for the groups of the canine population being considered, and differences in case definition when determining a positive result.[101] This could result in a gross underestimation of the prevalence within the general canine population or within specific breeds.[101]

Gonadectomy is a risk factor for development of CCL disease and hip dysplasia in both male and female dogs.[102–105] The complex pathophysiologic processes of these orthopedic diseases make it challenging to connect cause and effect.[105] Although heritability is the primary factor for the development of hip dysplasia, it is a multifactorial condition.[106] Hip dysplasia most commonly affects large-breed dogs. Similarly, most dogs treated for CCL disease are young, active, large-breed dogs.[106] Development of CCL disease may result from degenerative or traumatic causes.[106] Ligament degeneration has also been associated with aging, conformational abnormalities, and immune-mediated arthropathies.[106]

Investigators of 1 study[102] found an overall prevalence for CCL disease of 3.48%, with gonadectomized dogs having a significantly higher prevalence than their sexually intact counterparts, and neutered females having the highest prevalence. This supported results of another study[105] that revealed an increased prevalence of CCL disease in female dogs and that the age at the time of OHE did not appear to be a factor. The finding that large dogs were more likely to have CCL rupture is consistent throughout several studies.[102,103,105] A retrospective study[103] conducted to evaluate both musculoskeletal diseases found that gonadectomy increased the prevalence of CCL disease in male and female dogs and that hip dysplasia was more prevalent among neutered male dogs and less common among female dogs regardless of their neuter status.

Breed predisposition may also play a major role in the development of CCL disease and hip dysplasia.[5,6,14,101,103–105,107] Four breed-specific studies[5,6,14,107] revealed a significant increase in orthopedic disorders in gonadectomized dogs, compared with results for their sexually intact counterparts, although the incidence differed widely among breeds. Prepubertal gonadectomy of Golden Retrievers resulted in an increased incidence of joint disorders (3 to 5 times as high as the incidence for sexually intact dogs), whereas prepubertal gonadectomy of Labrador Retrievers was associated with an incidence that was twice as high as that for sexually intact dogs. The incidence of hip dysplasia increased significantly only in male Golden Retrievers neutered before 1 year of age. Elbow joint dysplasia increased significantly only for male Labrador Retrievers neutered before 6 months of age (incidence, 2%), compared with that for sexually intact males (incidence, 0.57%).[5,6] Boxers that were gonadectomized at least 6 months prior to diagnosis of hip dysplasia, (mean age at gonadectomy, 3 years) were 1.5 times as likely as sexually intact Boxers to develop hip dysplasia. Male and female German Shepherd Dogs gonadectomized before 12 months of age were at an increased risk for CCL tears, compared with the risk for those remaining sexually intact.[14] There was not a significant association between gonadectomy and hip dysplasia or elbow joint dysplasia in German Shepherd Dogs.[14] Prepubertal gonadectomy is associated with increased bone length attributable to delayed closure of growth plates.[108] Although it has been speculated that this subsequently leads to the development of certain orthopedic diseases, the speculated association has not been explained or confirmed.[14,15,28,34]

The effect of sex hormones on orthopedic disease has also been explored via comparisons between gonadectomy performed at early and traditional ages.[3,4] Comparison of outcomes for shelter dogs gonadectomized before or after 24 weeks of age revealed no association between age at gonadectomy and frequency of musculoskeletal problems during the 4 years after gonadectomy. A few dogs developed hip dysplasia, but they did not require surgical or prolonged medical management.[3] A similar study[4] for which follow-up monitoring was available for as long as 11 years after gonadectomy revealed a significant increase in the incidence of hip dysplasia among dogs gonadectomized before 5.5 months of age, compared with the incidence for those gonadectomized after 5.5 months of age. However, there was a lower rate for euthanasia among the early-age gonadectomized dogs with hip dysplasia.[4] Although neither of these studies included a comparison with sexually intact animals and it was unclear as to the diagnostic tests used to diagnose hip dysplasia, the low incidence and severity of orthopedic problems in prepubertally gonadectomized dogs makes it worthwhile to consider early-age neutering.[3,34]

Behavior

Inappropriate or unacceptable behaviors disrupt the human-animal bond and are one of the most common reasons for relinquishment or rehoming of dogs.[3,109] Because some owners pursue gonadectomy to prevent or resolve behavioral problems of their pets,[15,110–112] they should be given realistic expectations for potential postsurgical behavioral changes.

Gonadectomy and the resultant decrease in gonadal steroid hormones typically result in a marked reduction or elimination of sexually dimorphic behaviors, including roaming, hormonal aggression (fighting with other males or females), and urine marking.[2,15,28,29,110,112–114] In males, the age at castration or duration of the behavior does not change the likelihood that surgery will alter these unwanted behaviors.[113,114]

The literature provides consistent results regarding the effects of gonadectomy on behaviors driven by testosterone or estrogen; however, studies involving behaviors not directly related to gonadal steroid hormones have resulted in mixed findings. Although the most serious bite injuries in the United States involve sexually intact dogs,[115] gonadectomy has not been found to be a useful measure to prevent aggressive behavior in male or female dogs.[109,111,116,117] Gonadectomy consistently reduces only intermale aggression and may actually contribute to increased aggression in female dogs.[109,111,116–118] In a study[118] conducted to evaluate canine patients referred for management of behavioral problems, sexually intact males and neutered females were significantly more likely to be referred because of aggression and stimulus reactivity than were neutered males and sexually intact females. A prospective controlled study[117] of German Shepherd Dogs revealed increased reactivity to unfamiliar people and unknown dogs following OHE performed between 5 and 10 months of age, compared with results for dogs allowed to remain sexually intact. A study[116] based on responses of 150 owners of dogs to questionnaires administered at the time of spaying and again 6 months later revealed a significant increase in dominance aggression toward family members by bitches following OHE, compared with the response of sexually intact female dogs of similar age and breed assessed at the same time periods. Female puppies that already had displayed signs of aggression were at highest risk for an increase in dominance aggression following gonadectomy, and there was little risk of increased aggression in older dogs that had not already displayed aggressive behavior.[116] Therefore, consideration should be given to postponing OHE in female puppies with a history of aggression.

Differences in study designs and results create additional challenges when the potential consequences of gonadectomy on behavior are evaluated. Investigators of 1 study[110] reported decreased activity in 50% of male dogs neutered as adults, contrary to results of an earlier study[113] in which there was no indication that neutered male dogs become more inactive or lethargic. Additional differences were for dogs gonadectomized at 7 weeks or 7 months of age, which were judged to be more excitable than were sexually intact dogs.[108] When dogs gonadectomized before or after 5.5 months of age were compared, those neutered before 5.5 months of age were more likely to display noise phobias and sexual behaviors. However, separation anxiety, urination due to fear, and the likelihood a dog would escape were less likely.[4] Male puppies neutered prior to 5.5 months of age had increased aggression toward family members and also were more likely to bark excessively at visitors or household members.[4] In another study[3] conducted to evaluate gonadectomy in dogs before or after 24 weeks of age, investigators concluded that there was no increase in the incidence of behavioral problems or return rate to shelters for prepubertally gonadectomized dogs. Vizslas gonadectomized before 6 months of age reportedly have an increase of undesirable behaviors related to fear and anxiety.[36] Investigators of that study[36] did not evaluate sexual behaviors such as mounting and urine marking. When bitches of various breeds spayed between 2 and 4 years of age were compared with a sexually intact control group, no behavioral differences were observed during the 2 months after gonadectomy.[119]

Interpretation of the literature related to behavioral changes after gonadectomy is further complicated by various definitions of aggression as well as comparisons of similar-appearing but potentially unrelated behaviors (eg, aggression, reactivity or energy level, and excitability).[120] It is also possible that gonadectomy was recommended for some dogs as part of a behavior treatment plan, which would artificially increase the number of spayed or neutered dogs with behavioral problems.[28] Because of these complicating factors, additional research is needed before conclusions can be confidently made about the effects of gonadectomy beyond the reduction of reproductive behaviors. Specific evaluation of potential behavioral consequences of surgery during critical periods of behavioral development could help guide general recommendations on the most appropriate time for gonadectomy of puppies.[120–123]

Other Medical Implications

Gonadectomy can contribute to the prevalence (or be used in the management) of a variety of medical concerns. In male dogs, castration helps prevent androgen-related diseases, including BPH, chronic prostatitis, perianal adenomas, and perianal hernias.[28,29,34,124,125] Benign prostatic hyperplasia is the most common prostatic disorder among sexually intact male dogs, potentially affecting 50% of sexually intact dogs by 5 years of age and 95% to 100% of sexually intact dogs > 9 years old.[29,34,66,124,125] Dogs with BPH are predisposed to prostatic cysts, prostatitis, and prostatic abscesses.[66,67,124,125] In a study[67] of multiple prostatic disease processes, BPH was found to be by far the most common prostatic abnormality associated with clinical signs of prostatic disease. Signs of prostatic disease most often include urethral discharge, hematuria, or tenesmus.[66,124,125] Castrated dogs accounted for only 6.7% of the dogs with a nonmalignant prostatic disorder (OR, 0.28).[67] Castration is the recommended treatment for most dogs with clinical BPH and results in a decrease in the size of the prostate, regression of clinical signs, and a reduced likelihood of developing infectious prostatitis.[28,29,34,61,67,124,125] The prognosis following castration is excellent.[29]

For females, other benefits of OHE include prevention and treatment of disorders of the reproductive tract, including pyometra, metritis, and ovarian cysts as well as conditions associated with pregnancy and parturition (eg, dystocia).[15,29,34,126] Pyometra is a potentially life-threatening condition often associated with cystic endometrial hyperplasia.[29] In countries in which OHE is not as routinely performed as in the United States, the mean incidence of pyometra can be 23% to 24% of dogs by 10 years of age.[127] In a study[46] that involved examination of ovarian tumors, 43% of the dogs had a medical history consistent with pyometra. Similar to other disease processes, the incidence of pyometra may differ among breeds.[6,127,128] An OHE is the recommended treatment for pyometra in most cases because medical management may not completely clear infection and cannot reverse cystic endometrial hyperplasia.[127,128] Furthermore, subsequent estruses could result in recurrent pyometra (estimated rate, 20%[29] or 10% to 77%[128]). Septic shock and renal failure are potential sequelae of pyometra.[29,128] Mortality rates of 4.2% to 4.3%[127] and 0% to 17%[28] have been reported for dogs. Emergency treatment of pyometra also necessitates unexpected and potentially substantial financial commitments by owners.

Acquired urinary incontinence is consistently cited as a potential sequela to spaying female dogs. Urinary incontinence typically develops 3 to 5 years after gonadectomy.[129–132] It affects 2% to 20% of spayed females and occurs most often in larger dogs.[129–132] Females spayed before 3 months of age have the highest risk of developing urinary incontinence that requires medical treatment.[4,131] Spaying females between 4 and 6 months of age does not appear to increase the risk for urinary incontinence, compared with the risk for those spayed after the first estrus.[4,131] Age at gonadectomy may also influence time to onset of urethral incompetence, with a shorter interval to incontinence reported for bitches spayed when they were older.[132]

A breed-specific study[21] on German Shepherd Dogs found that urinary incontinence was considerably less likely to develop in sexually intact females. However, this was only a significant effect when sexually intact females were compared with female dogs spayed between 6 and 11 months of age. The author's conclusion[21] that dogs spayed before 6 months of age or considered as a group spayed prior to 12 months of age were not at an increased risk for the development of urinary incontinence conflicts with the previously reported[4,14] increased risk attributable to early-age gonadectomy. Although the information from that study[21] supports the association between gonadectomy and acquired urinary incontinence, it may complicate recommendations regarding the most appropriate age at which to spay a German Shepherd Dog.

Urinary incontinence can negatively affect some owner-animal relationships; however, it is important to mention that none of the female dogs with urinary incontinence in studies[4,131] on early-age gonadectomy were relinquished to a shelter or given to another owner, and the euthanasia rate of these dogs was not higher than the overall euthanasia rate. This may be because patients typically respond well to medical management or because urinary incontinence may not be viewed by owners as a sufficient inconvenience or impairment to consider relinquishment.[3,28,130–133] Investigators of a recent systematic review[134] categorized the causal relationship between gonadectomy and urinary incontinence as weak. However, similar to the previously mentioned systematic review on mammary gland neoplasia and gonadectomy,[41] information must be weighed with the acknowledgment that a lack of qualifying literature will negatively impact the statistical power of such a systematic analysis.

It is estimated that obesity affects 24% to 30% of the pet population in the United States.[135] Retrospective studies[28,136] have consistently found an increase in body condition in dogs after gonadectomy. This appears to be a result of both an increase in appetite and changes in metabolism.[137] It is unclear whether age at gonadectomy plays a major role in the risk of a neutered dog becoming overweight, but there appears to be an increased risk, compared with that for sexually intact dogs, for patients primarily from 2 months to 2 years after surgery.[4,119,136] Although obesity remains a challenge in companion animal medicine, it is a multifactorial problem, and responsible management of diet and exercise can maintain appropriate body condition regardless of neuter status.[28,34]

Lifespan

Overall, gonadectomy appears to be associated with an increase in lifespan.[15,34,38,138–140] This has great importance for veterinary medicine, whereby euthanasia is considered when quality of life is substantially compromised and cannot be expected to reasonably improve. A retrospective study[38] that included data from the VMDB found that neutering was strongly associated with an increased lifespan (life expectancy of spayed females was increased by 26.3%, and that of castrated males was increased by 13.8%). Although gonadectomy increased the risk of death attributable to neoplasia (except for mammary gland neoplasia, which had a significantly lower prevalence) and immune-mediated disease, it decreased the risk of death attributable to other causes, including infectious disease and trauma.[38] Similarly, analysis of patient data evaluated in a 2013 report[138] that included data from primary care veterinary hospitals revealed that spayed dogs typically lived 23% longer and neutered dogs lived 18% longer than did sexually intact female and male dogs, respectively. That report[138] also revealed that sexually intact dogs were more than twice as likely as gonadectomized dogs to be hit by a car or bitten by another animal. Results of a survey of owners of > 3,000 British dogs indicated that spayed females lived significantly longer than did males and sexually intact females.[139]

For military working dogs, neutered males lived significantly longer than sexually intact males and spayed females.[140] The study population did not have any sexually intact female dogs for comparison, and the age at gonadectomy was not considered. Degenerative joint disease of the appendicular skeleton and neoplasia were the leading causes of death or reasons for euthanasia, affecting 19.2% and 18.3% of the population of military working dogs, respectively.[140] Deaths associated with gastric dilatation–volvulus (9.1% of the population) resulted in an OR twice as high for gonadectomized males and females as for sexually intact males. This differed from results of other studies[141,142] that indicated the risk of gastric dilatation–volvulus was not associated with neuter status. Lifespan, cause of death, and reason for euthanasia differ among breeds.[140]

A retrospective study[143] conducted to evaluate necropsy data from dogs revealed that the mean age at death did not differ significantly between gonadectomized and sexually intact dogs of both sexes. However, there were marked differences in longevity among breeds.[143] Gonadectomized male and female Rottweilers lived longer than sexually intact Rottweilers in a cohort evaluated for osteosarcoma,[7] but a separate longevity study[144] found that females spayed after 4 years of age were more likely to reach 13 years of age. Although the retrospective cohort study[36] of Vizslas found significantly higher odds that gonadectomized dogs would have neoplasia than would sexually intact Vizslas, that same study did not reveal a significant difference in longevity or age at death between sexually intact and gonadectomized dogs.

Population Management

The AVMA concludes that dog and cat population control is a primary welfare concern of society.[145] There have been improvements in many geographic areas, but the population of dogs in the United States still substantially exceeds the capacity of society to care and provide homes for all of them.[145] It is estimated that millions of dogs are euthanized at animal shelters in the United States each year, and over half of canine litters in US households are unplanned.[4,15,28,146] Reducing unplanned and indiscriminant breeding through gonadectomy is an effective means of non-lethal population management.[2,145,147,148] Society benefits from elective gonadectomy because animal overpopulation is reduced, which results in fewer animals relinquished to humane organizations.[28] Local ordinances regulating gonadectomy of dogs must also be considered.

Ownership and the population of animals play a role in the assessment for the appropriateness of gonadectomy.[11,145] It is imperative that dogs rehomed through humane organizations do not contribute further to overpopulation.[145] Unfortunately, noncompliance with spay-neuter contracts is as high as 60%.[15,28,146] Gonadectomy performed before a dog reaches sexual maturity or is adopted can address the issue of owner compliance, ameliorate animal overpopulation, and prevent the birth of unintended litters.[4,147–149] Analysis of the current literature reveals that there is minimal risk for surgical complications or subsequent developmental abnormalities between pediatric gonadectomy performed on dogs between 6 and 14 weeks of age and gonadectomy performed on dogs at the more traditional age of 6 months, both of which are prior to puberty.[3,4,28,29,146–148,150]

Anesthetic and Surgical Complications

Gonadectomy is an elective procedure, and the risk of anesthetic and surgical complications must be considered along with the previously mentioned long-term risks and benefits with or without gonadal hormones. When a surgical candidate is evaluated for gonadectomy, a veterinarian must consider age, body weight, and existing medical conditions that may increase the risk of anesthetic or surgical complications.[150] Potential complications of soft tissue surgery and anesthesia include hemorrhage, hypothermia, pain, wound inflammation, delayed wound healing, dehiscence, and death.[29,150–154] Studies[28,152,153] based on veterinary students performing OHE and castration have found complication rates of 20% to 30%, but the most common complications were considered minor problems, and the rate of occurrence was thought to be influenced by the experience of the person performing the surgery. Complications can be minimized through appropriate patient selection, use of safe and efficient protocols for anesthesia, application of minimally traumatic patient preparation and surgical techniques, careful monitoring of patients, and multimodal pain management including preoperative analgesia.[150,154,155]

Potential Areas for Future Study

Potential associations between neuter status and other disease processes including adrenal gland disease, hypothyroidism, cognitive function, and patellar luxation have been discussed. Adrenal gland tumors and nodular hyperplasia have been associated with gonadectomy in ferrets, but no associations currently have been made between adrenal gland disease and gonadectomy in dogs.[15,28] Literature on the association between neuter status and hypothyroidism has provided mixed results, with an association indicated in some reports[156,157] and no association indicated in other reports.[4,158,159] Currently, there is insufficient support for an association between gonadectomy and an increased risk of hypothyroidism in dogs.[15,34]

The situation is similar for cognitive dysfunction. In 1 study[160] conducted to evaluate the potential effect of neuter status on cognitive function, neutered male dogs were more likely to progress from mild to severe cognitive impairment than were sexually intact male dogs. The study[160] did not have a sufficient number of sexually intact female dogs for evaluation, and only 6 sexually intact male dogs were available for the final comparison. In contrast, investigators of a study[161] on the effects of testosterone on longevity in humans and dogs suggested that orchiectomy may reduce DNA damage within the brain of elderly Beagles. However, the study[161] sample size was small, with only 4 dogs in each group. Neither neuter status nor age at gonadectomy has been found to affect trainability of working dogs.[28]

Patellar luxation is unrelated to age at gonadectomy, but gonadectomized dogs may be at an increased risk for patellar luxation, compared with the risk for sexually intact dogs.[4,162] A study[162] conducted to evaluate diagnostic and genetic aspects of patellar luxation found that body weight, age, and neuter status were associated with patellar luxation. Because the gonadectomized dogs of that study[162] were significantly older than the sexually intact dogs, the author stated that the role (if any) of gonadectomy in the mechanisms leading to patellar luxation could not be deduced from the data. Age at gonadectomy of the dogs was also unknown.[162] Continued research into these potential associations appears to be warranted. However, analysis of the literature currently does not justify considering these diseases when making clinical decisions about if or when to spay or neuter a canine patient.

Clinical Relevance

Routine gonadectomy of companion animal dogs is a commonly accepted procedure in the United States. The widespread recommendation for gonadectomy is based on advocating for the welfare of the animal as well as the general canine population by reducing the incidence of certain medical problems and minimizing contributions to the homeless animal population. In addition to these benefits, gonadectomy also has the potential to affect an individual dog's risk of certain diseases and disorders. Although information about the risks associated with gonadectomy has been reported in the past, the recommendation for gonadectomy as a blanket policy is increasingly controversial, with greater focus on possible ramifications for individual animals in addition to the canine population as a whole. These risks and benefits must be revisited as new information becomes available. Because of the substantial national problem of homeless animals, shelter and rescue organizations are encouraged to spay and neuter dogs prior to adoption to prevent those animals from further contributing to the population of unwanted animals.[145,147] Similar to other areas of veterinary medicine, it is the responsibility of veterinarians to use their best medical judgment (on the basis of each animal's ownership, breed, sex, and intended use) to weigh both the potential risks and benefits when determining whether gonadectomy is appropriate and, if so, the appropriate age for the surgery.[2,11,34,36,147,149]

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